MUSCULOSKELETAL PHYSIOLOGY

Fatima Daoud, MD, PhD

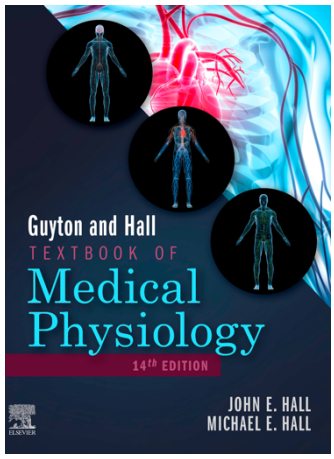
Office hours: 12:30-1:30

Faculty of medicine, building 1, 3rd floor, 327.

Feel free at anytime to contact me via Teams.

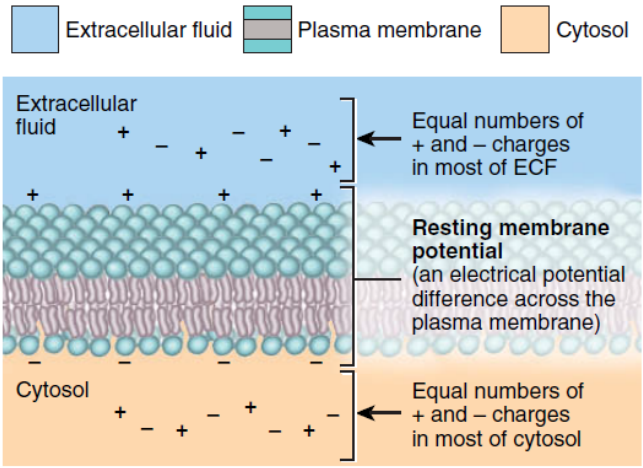
Chapter 6: Contraction of Skeletal Muscle

Chapter 7. Excitation of Skeletal Muscle: Neuromuscular Transmission and Excitation-Contraction Coupling

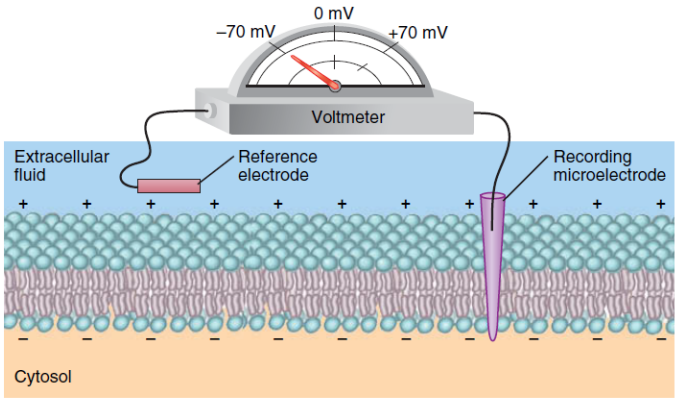


Revision

RESTING MEMBRANE POTENTIAL

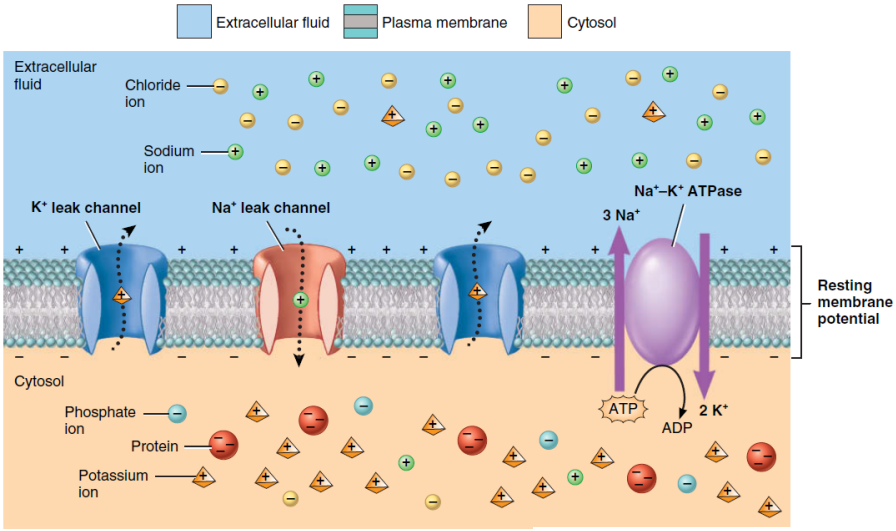


(a) Distribution of charges that produce the resting membrane potential of a neuron



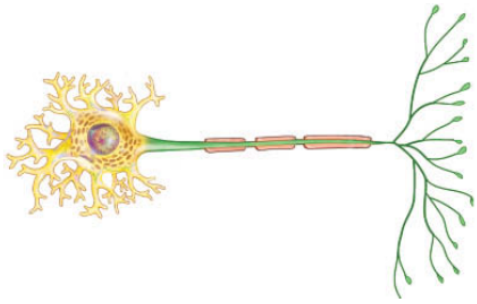
(b) Measurement of the resting membrane potential of a neuron

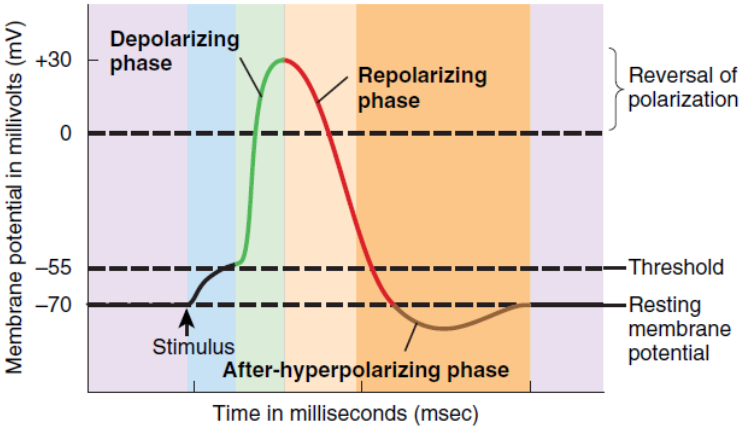
RESTING MEMBRANE POTENTIAL



Nerve action potential

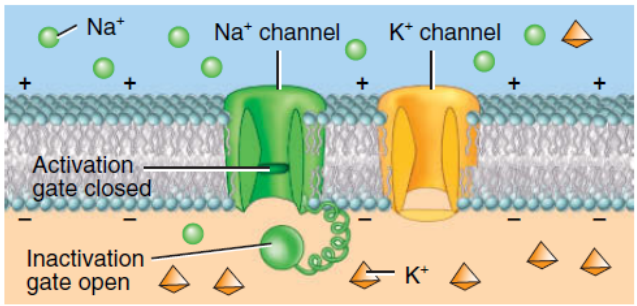
Rapid changes in the membrane potential that spread rapidly along the nerve fiber membrane.

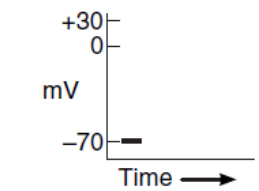




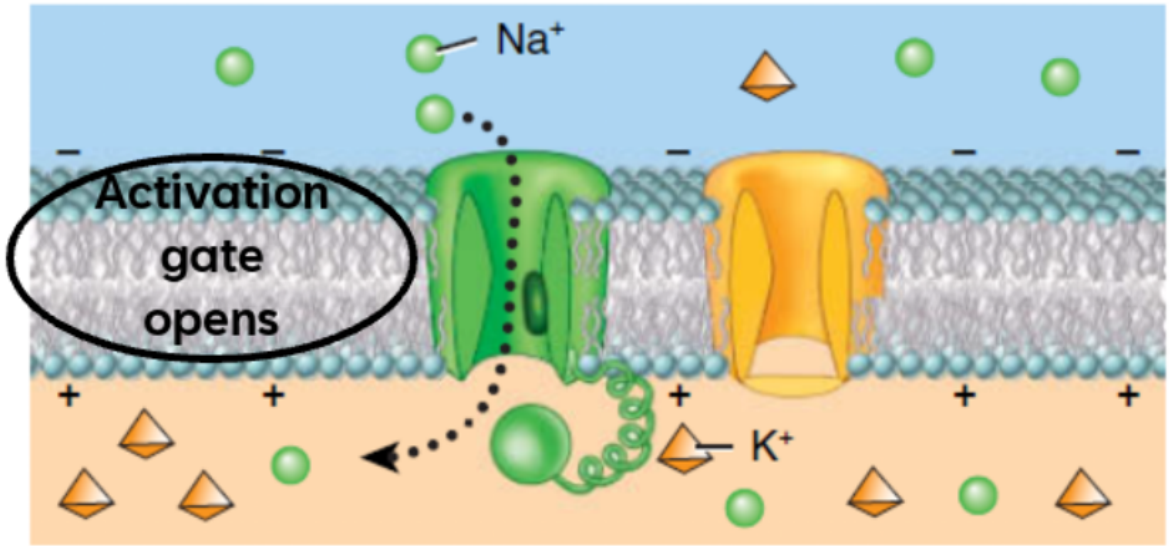
- Resting membrane potential: Voltage-gated Na^+ channels are in the resting state and voltage-gated K^+ channels are closed
- Stimulus causes depolarization to threshold
- Voltage-gated Na^+ channel activation gates are open
- Voltage-gated K^+ channels are open; Na^+ channels are inactivating
- Voltage-gated K^+ channels are still open; Na^+ channels are in the resting state

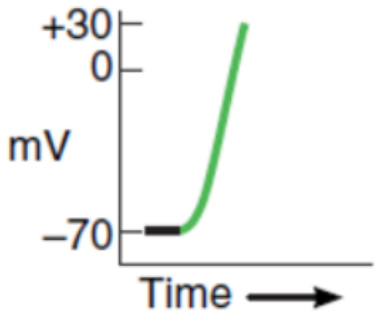
1. **Resting state:**
   All voltage-gated Na^+ and K^+ channels are closed. The axon plasma membrane is at resting membrane potential: small buildup of negative charges along inside surface of membrane and an equal buildup of positive charges along outside surface of membrane.



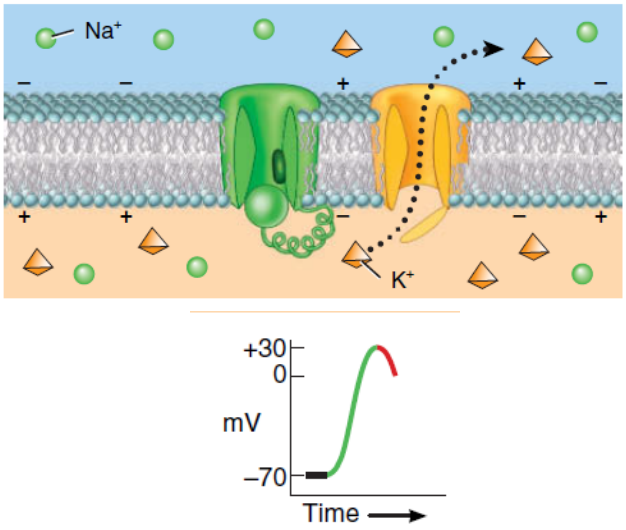


2. **Depolarizing phase:**
When membrane potential of axon reaches threshold, the Na^+ channel activation gates open. As Na^+ ions move through these channels into the neuron, a buildup of positive charges forms along inside surface of membrane and the membrane becomes depolarized.

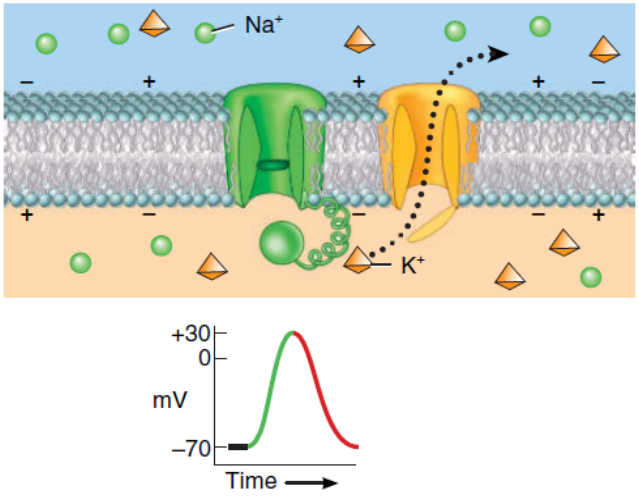




3. **Repolarizing phase begins:** Na^+ channel inactivation gates close and K^+ channels open. The membrane starts to become repolarized as some K^+ ions leave the neuron and a few negative charges begin to build up along the inside surface of the membrane.



4. **Repolarization phase continues:** K^+ outflow continues. As more K^+ ions leave the neuron, more negative charges build up along inside surface of membrane. K^+ outflow eventually restores resting membrane potential. Na^+ channel activation gates close and inactivation gates open. Return to resting state when K^+ gates close.



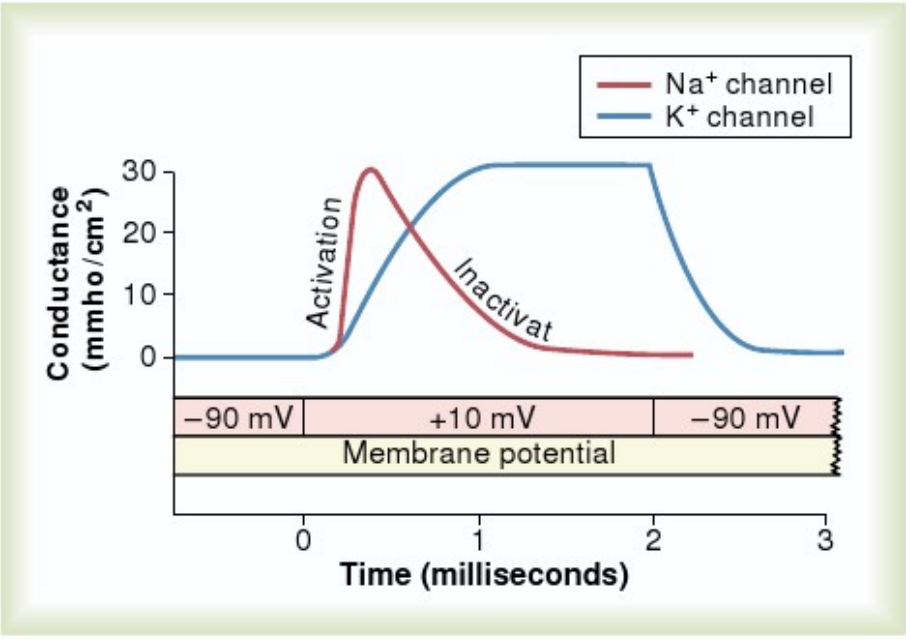
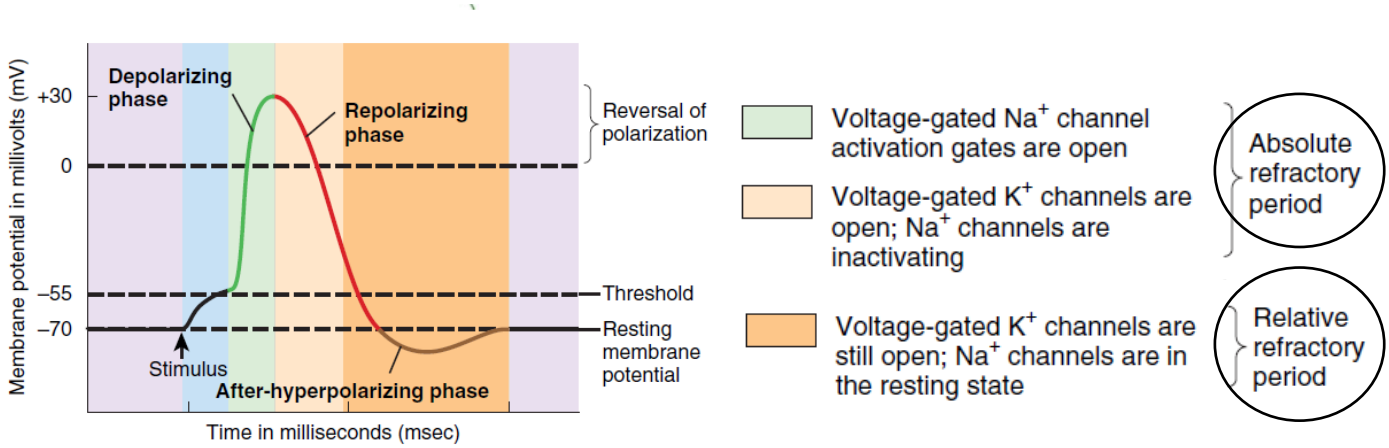
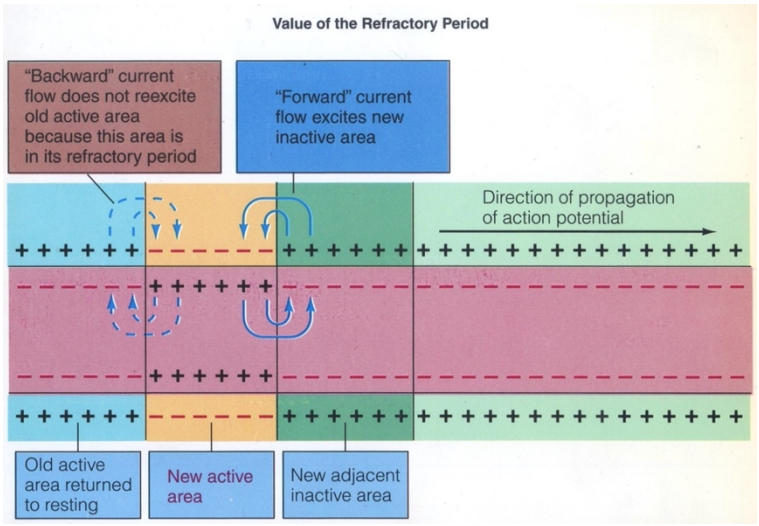


Figure 5–9

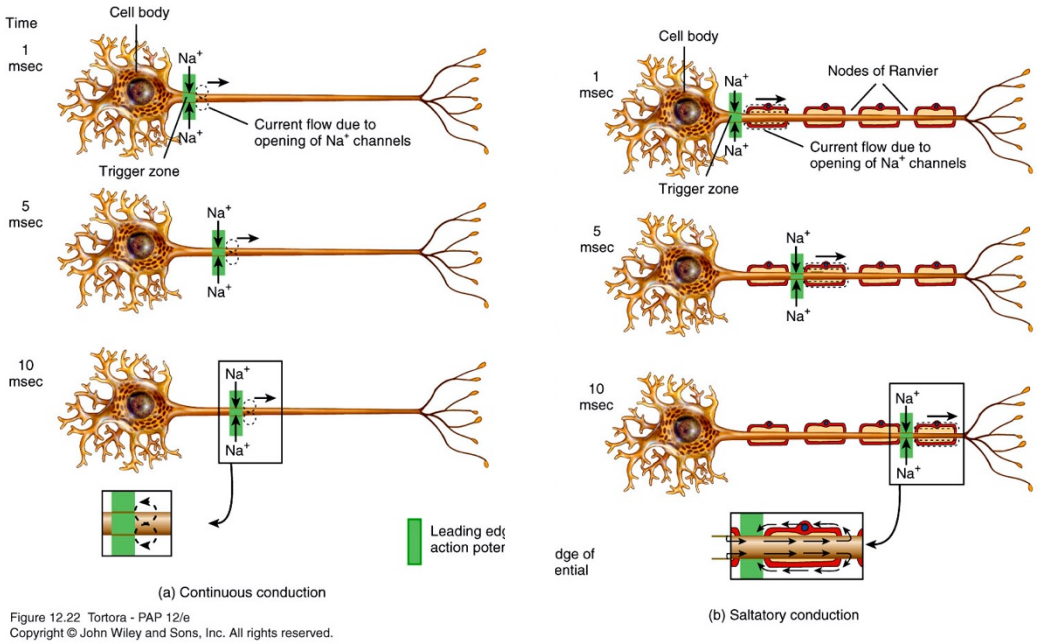
Refractory period



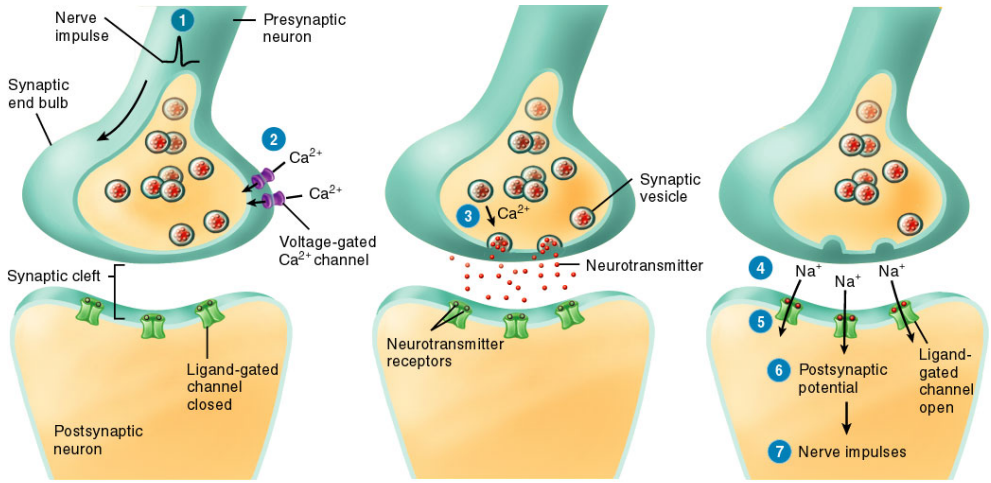
ACTION POTENTIAL PROPAGATION



TYPES OF ACTION POTENTIALS PROPAGATION



SIGNAL TRANSMISSION AT SYNAPSES



12.14

EXCITATORY AND INHIBITORY POSTSYNAPTIC POTENTIALS

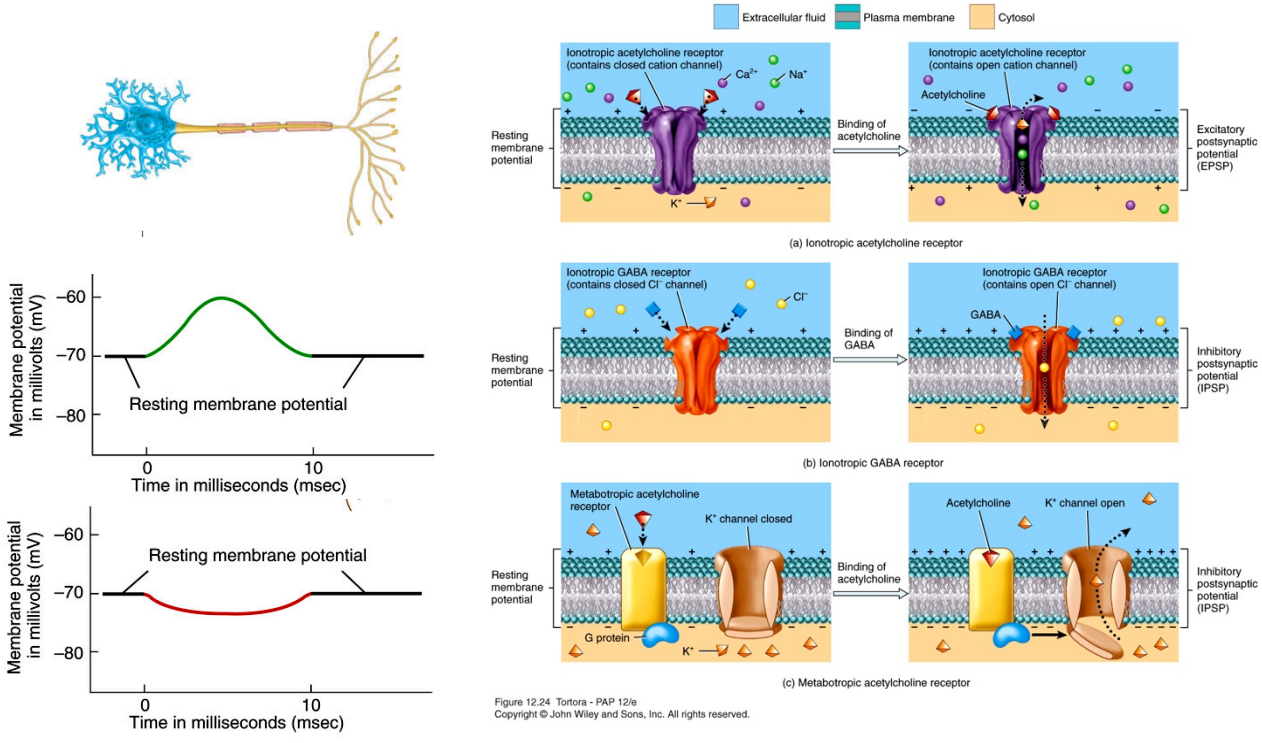
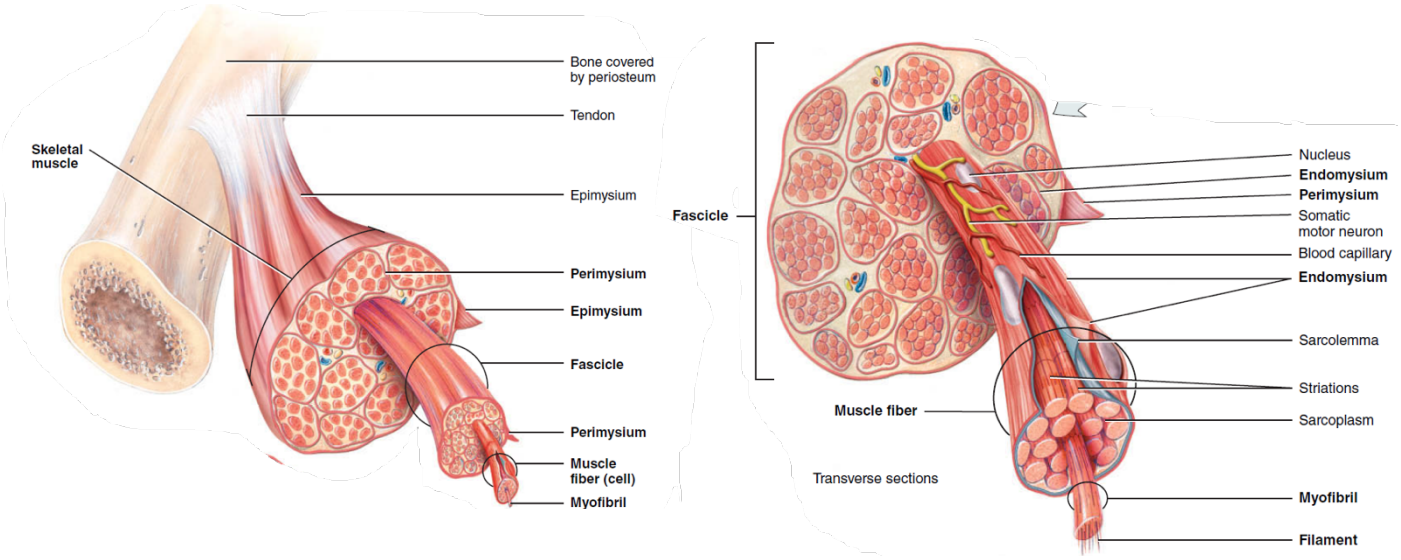


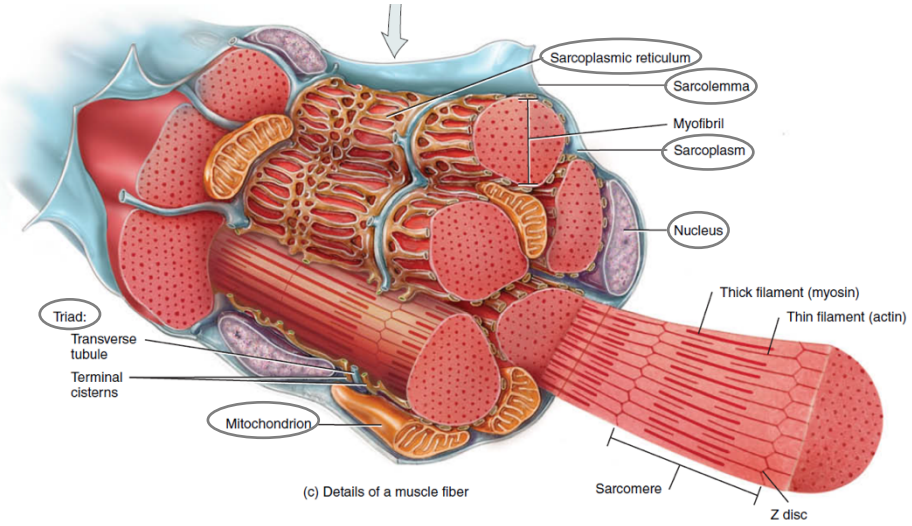
Figure 12.24 Tortora - PAP 12/e

SKELETAL MUSCLE

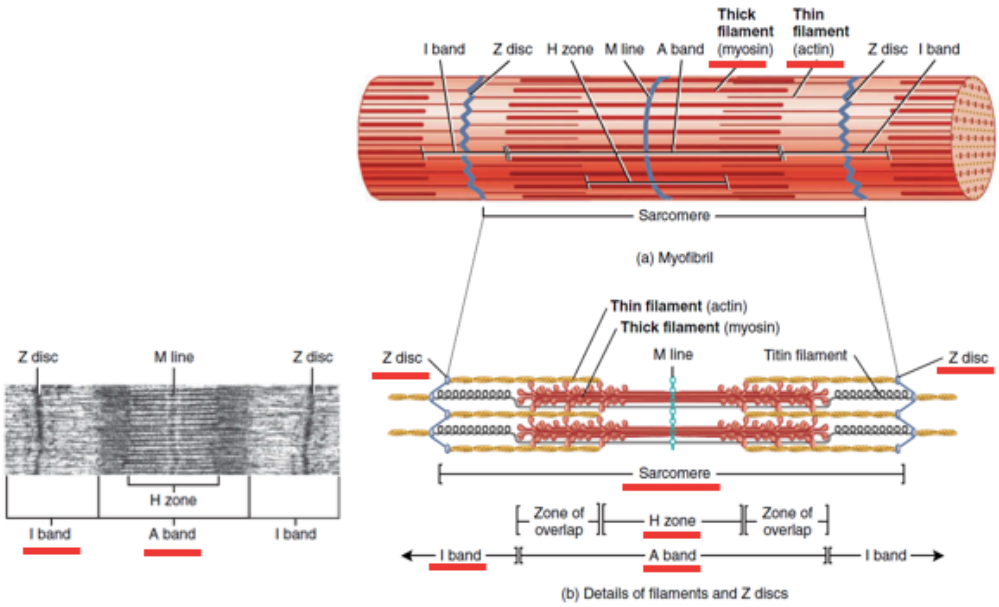
structure



Skeletal muscle tissue consists of long, cylindrical, striated fibers (striations are alternating light and dark bands within fibers that are visible under a light microscope). Skeletal muscle fibers vary greatly in length, from a few centimeters in short muscles to 30–40 cm (about 12–16 in.) in the longest muscles. A muscle fiber is a roughly cylindrical, multinucleated cell with nuclei at the periphery. Skeletal muscle is considered voluntary because it can be made to contract or relax by conscious control. Location: Usually attached to bones by tendons. Function: Motion, posture, heat production, protection.



- The sarcolemma consists of a true cell membrane, called the plasma membrane, and an outer coat made up of a thin layer of polysaccharide material that contains numerous thin collagen fibrils. At each end of the muscle fiber, this surface layer of the sarcolemma fuses with a tendon fiber. The tendon fibers, in turn, collect into bundles to form the muscle tendons that then connect the muscles to the bones.
- The spaces between the myofibrils are filled with intracellular fluid called sarcoplasm, containing large quantities of potassium, magnesium, and phosphate, plus multiple protein enzymes.
- There is tremendous numbers of mitochondria that lie parallel to the myofibrils. These mitochondria supply the contracting myofibrils with large amounts of energy in the form of adenosine triphosphate (ATP) formed by the mitochondria.
- Sarcoplasmic reticulum has a special organization that is extremely important in regulating calcium storage, release, reuptake and therefore muscle contraction

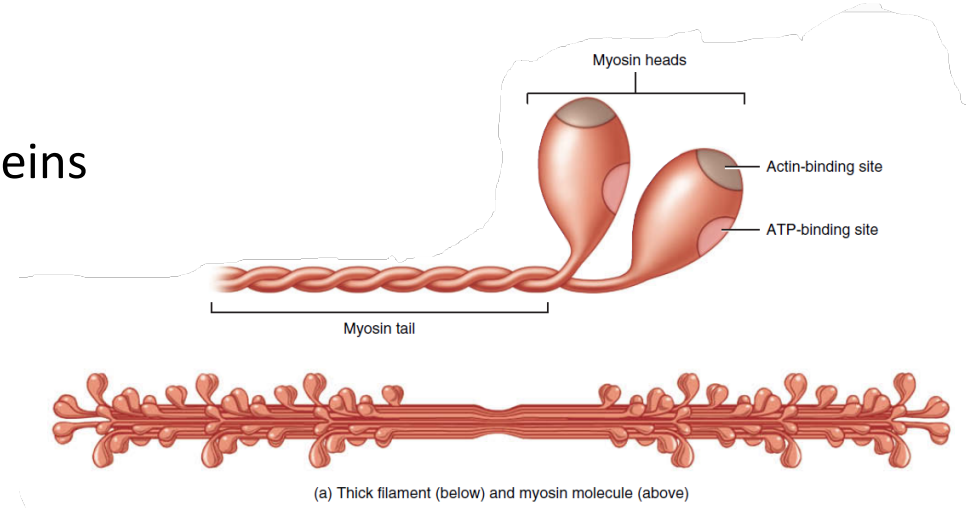


**Each muscle fiber contains several hundred to several thousand myofibrils.
** Each myofibril is composed of about 1500 adjacent myosin filaments and 3000 actin filaments, which are large polymerized protein molecules that are responsible for the muscle contraction.
** The light bands contain only actin filaments and are called I bands because they are isotropic to polarized light.
** The dark bands contain myosin filaments, as well as the ends of the actin filaments, where they overlap the myosin, and are called A bands because they are anisotropic to polarized light

---

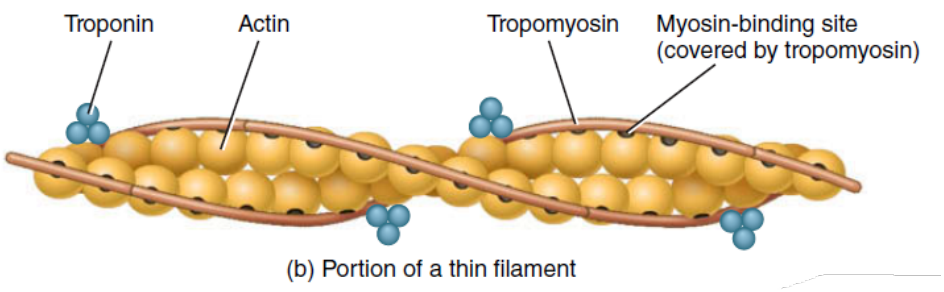
Contractile Proteins

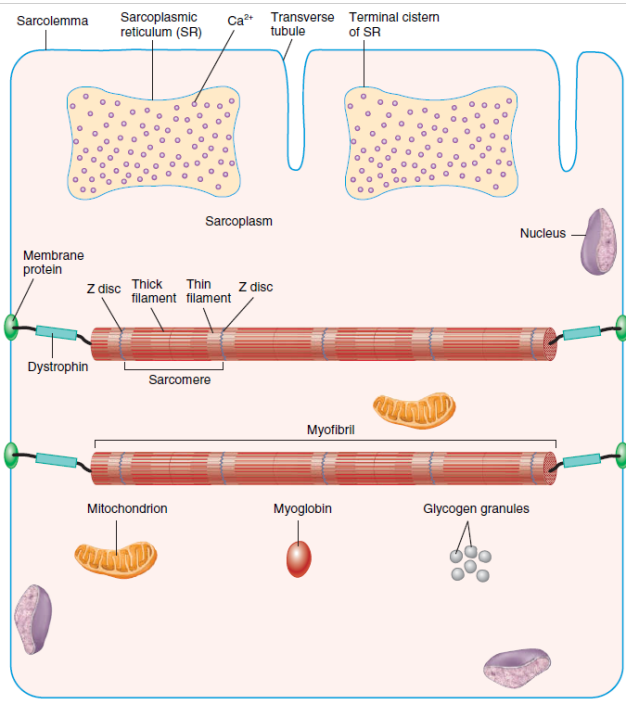
Myosin



Contractile Proteins

Actin





(d) Simplistic representation of the components of a muscle fiber

---

SKELETAL MUSCLE

Contraction _ sliding filaments

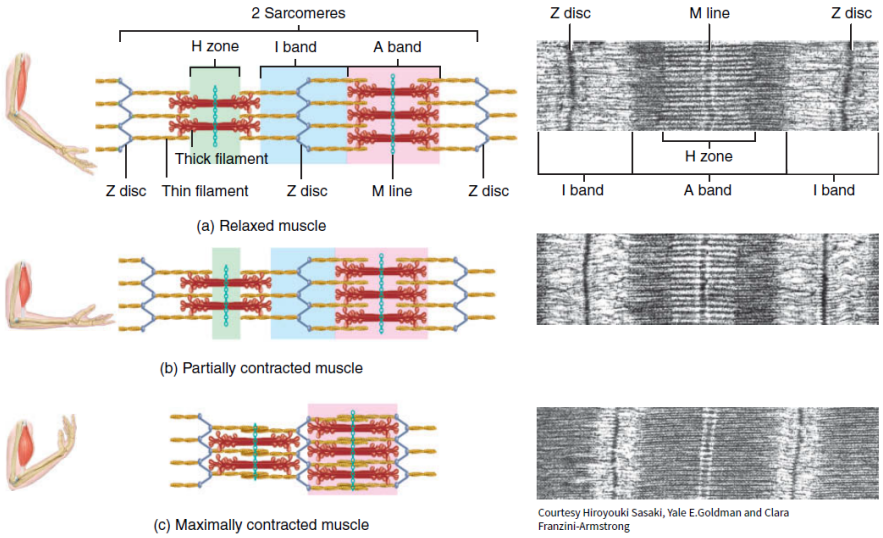
The Sliding Filament Mechanism

**Muscle contraction occurs because myosin heads attach to and "walk"

along the thin filaments at both ends of a sarcomere, progressively pulling

the thin filaments toward the M line.

**As a result, the thin filaments slide inward and meet at the center of a

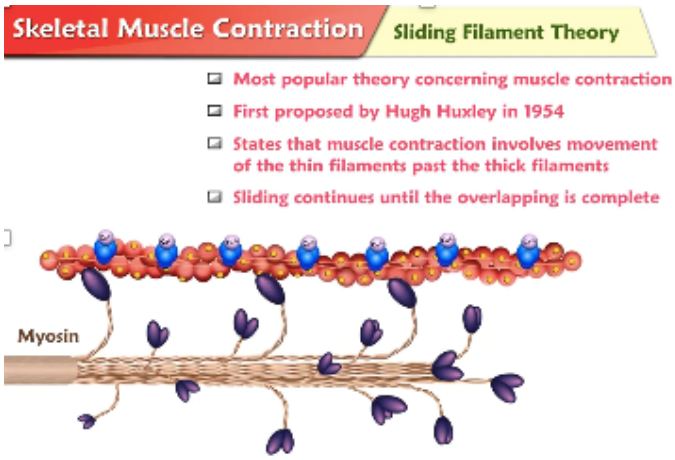


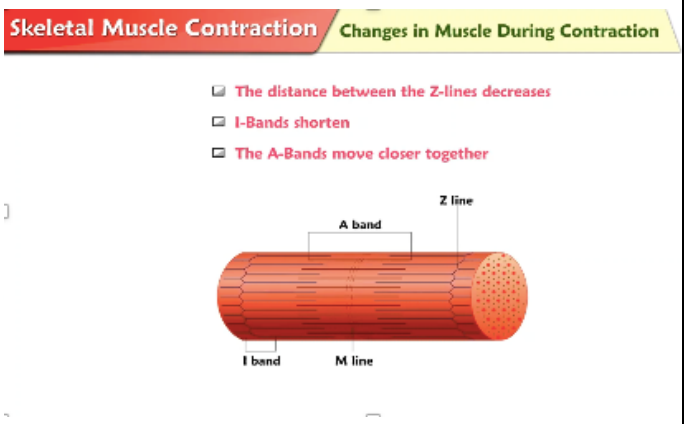
Courtesy Hiroyouki Sasaki, Yale E.Goldman and Clara Franzini-Armstrong

As the thin filaments slide inward, **the I band and H zone narrow and eventually disappear altogether when the muscle is maximally contracted

Since the thin filaments on each side of the sarcomere are attached to Z discs, when the thin filaments slide inward, **the Z discs come closer together, and the **sarcomere shortens**.

****Shortening of the sarcomeres causes shortening of the whole muscle fiber, which in turn leads to shortening of the entire muscle**.

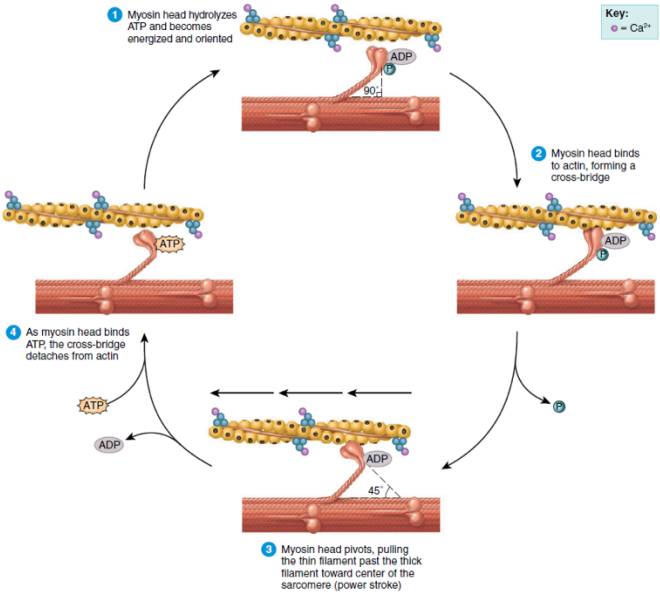




SKELETAL MUSCLE

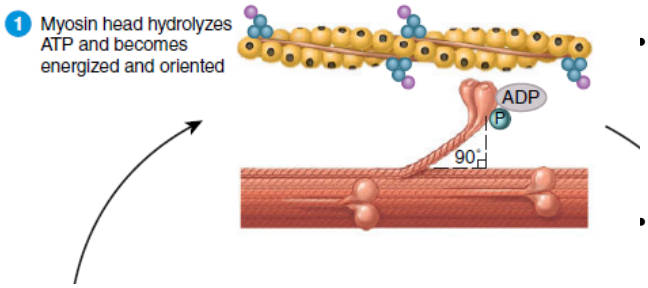
Contraction _ contraction cycle

THE CONTRACTION CYCLE



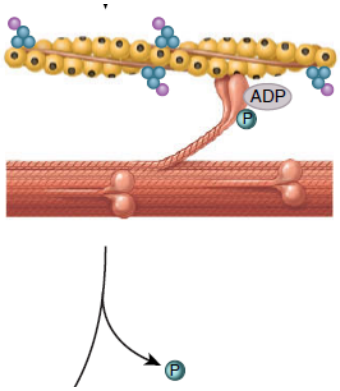
At the onset of contraction, the sarcoplasmic reticulum releases calcium ions (Ca2+) into the sarcoplasm. There, they bind to troponin. Troponin then moves tropomyosin away from the myosin-binding sites on actin. Once the binding sites are “free,” the **contraction cycle**—the repeating sequence of events that causes the filaments to slide—begins.

STEP 1: ATP HYDROLYSIS



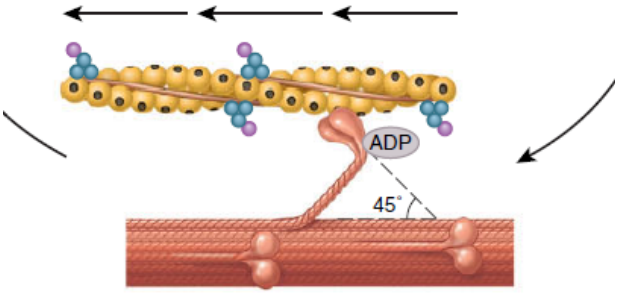
- The energy generated from ATP hydrolysis reaction is stored in the myosin head.
- The energized myosin head is perpendicular (at a 90° angle) relative to the thick and thin filaments and has the proper orientation to bind to an actin molecule.
- Notice that ADP and a phosphate group are still attached to the myosin head.

STEP 2: ATTACHMENT OF MYOSIN TO ACTIN



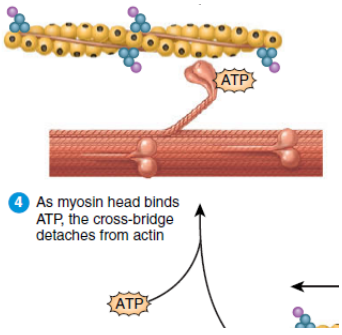
- The energized myosin head attaches to the myosin-binding site on actin and releases the phosphate group.
- When a myosin head attaches to actin during the contraction cycle, the myosin head is referred to as a **cross-bridge**.

STEP 3: POWER STROKE



- After a cross-bridge forms, the myosin head pivots, changing its position from a 90° angle to a 45° angle.
  As the myosin head changes to its new position, it pulls the thin filament past the thick filament toward the center of the sarcomere, generating tension (force). This event is known as the **power stroke**.
  Once the power stroke occurs, ADP is released from the myosin head.

STEP 4: DETACHMENT OF MYOSIN FROM ACTIN



- At the end of the power stroke, the cross-bridge remains firmly attached to actin until it binds another molecule of ATP.
- As ATP binds to the ATP binding site on the myosin head, the myosin head detaches from actin.

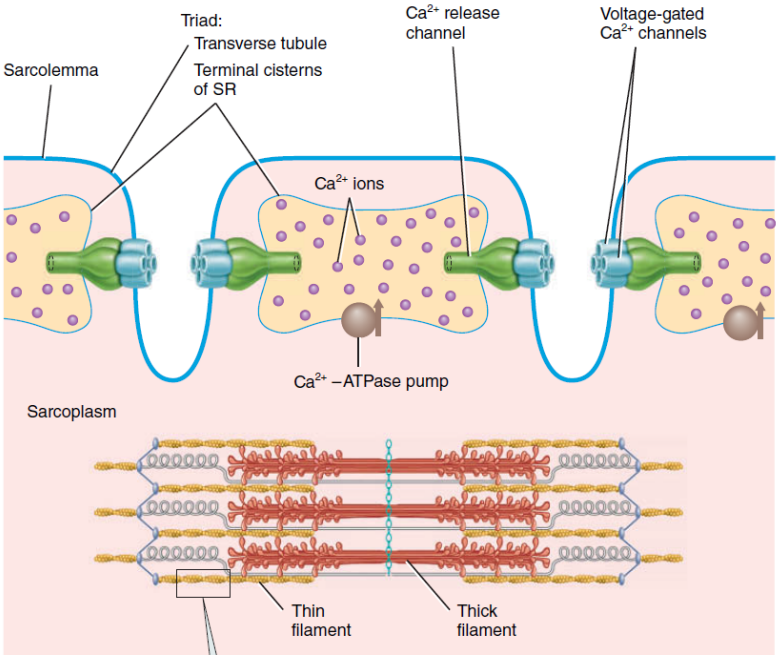
The contraction cycle repeats as the myosin ATPase hydrolyzes the newly bound molecule of ATP, and **continues as long as ATP is available and the Ca2+ level near the thin filament is sufficiently high.

Rigor Mortis (Rigidity of death)

- A condition in which muscles are in a state of rigidity.
- Begins 3–4 hours after death and lasts about 24 hours.
- Explanation : after death, cellular membranes become leaky. Calcium ions leak out of the sarcoplasmic reticulum into the sarcoplasm and allow myosin heads to bind to actin.
- ATP synthesis ceases shortly after breathing stops, however, so the cross-bridges cannot detach from actin.
- It disappears as proteolytic enzymes from lysosomes digest the cross-bridges.

SKELETAL MUSCLE

Relaxation



The terminal cisternal membrane of the sarcoplasmic reticulum also contains **Ca2+-ATPase pumps that use ATP to constantly transport Ca2+ from the sarcoplasm into the SR . As long as muscle action potentials continue to propagate along the T tubules, the Ca2+ release channels remain open and Ca2+ flows into the sarcoplasm faster than it is transported back into the SR by the Ca2+-ATPase pumps.

After the last action potential has propagated throughout the T tubules, the Ca2+ release channels close. As the Ca2+-ATPase pumps move Ca2+ back into the SR, the Ca2+ level in the sarcoplasm rapidly decreases.